

REMARKS

Group IV (Claims 14-17) has been elected. The specification has been amended to correct typographical errors.

No new matter has been added.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 300622005500. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

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EXHIBIT A: VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Please amend paragraph 48 of the specification as follows:

In an illustrative embodiment, the polyketide database consists of the polyketides described in current literature (Journal of Antibiotics (1981-present), Journal of Natural Products) and various databases (Chemical Abstracts CAPlus, AntiBase). All unique macrocyclic polyketides are converted to the modified CHUCKLES format. Of the [-]~1000 novel polyketides obtained, only [-]~200 different strings of monomers and unique macrocycles are needed to represent the much larger collection of polyketides in the database, because many of the differences between the naturally-occurring polyketides are due to different glycosyl (sugar) groups attached at different positions on the macrocycle.

Please amend paragraph 55 of the specification as follows:

Thus, the present invention provides methods and computational analysis tools for designing PKS genes to produce a desired polyketide. As an illustrative example, the present invention provides a computer program termed MORPH (see the Examples below) that can read the coded library (see the Examples below). An illustrative coded library consists of [-]~200 unique polyketide CHUCKLES strings. The user specifies the target polyketide, which is converted from molecular structure to a CHUCKLES string.

Please amend paragraph 69 of the specification as follows:

From even a modest library of [-]~200 compounds, one can in this manner generate using the methods of the invention, two to three times as many valuable chemical intermediates. Once such an intermediate is identified, the organism that produces the polyketide from which the

fragment is derived is fermented, the polyketide isolated in bulk, the chemical reaction performed, and the desired degradation product(s) isolated and used. In this manner, the present invention makes available a wide variety of useful products otherwise unattainable.

Please amend paragraph 76 of the specification as follows:

MORPH in its current implementation operates at the monomer level and thus does not handle intra-modular modifications/splitting. Future implementations could convert the CHUCKLES-encoded strings into the corresponding and equivalent SMILES and then perform more complex chemical analysis of the PKS molecular graphs. Currently, inter-modular double bonds are present in the library, but are ignored by the program. These bonds can be introduced post-biosynthetically and the exact source is generally unknown.